IFW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	**Office of Petitions**
Suman Preet Singh Khanuja et al.	Group Art Unit:
Application No.: 10/822,790	Examiner:
Filed: April 13, 2004	Confirmation No.: 3252
For: USE OF BIOACTIVE FRACTION FROM COW URINE DISTILLATE ('GO-MUTRA') AS A BIO-ENHANCER OF ANIT-INFECTIVE, ANTI-CANCER AGENTS AND NUTRIENTS	

SECOND PETITION PURSUANT TO 37 C.F.R. § 1.17(h)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Decision on Petition mailed on September 21, 2004, concerning Applicants' Petition to withdraw the Notice of Incomplete Nonprovisional Application filed under 37 C.F.R. § 1.53(b) Applicants provide the following remarks and the attached copies of parent application (Serial No. 10/135,763 filed on May 1, 2002) as filed and its date-stamped postcard.

As explained in Applicants' Petition filed on August 13, 2003, the Notice indicates that a filing date has not been accorded to the above-identified application because "the application was deposited without drawings." Applicants submit that even if this were correct, Applicants Request for Filing Continuation/Divisional Application Under 37 C.F.R. § 1.53(b) states at page 1, that the "entire disclosure of the prior application from which a copy of the oath or declaration is supplied herewith is considered as being a part of the disclosure of the accompanying application and

10/01/2004 GWORDOF1 00000073 10822790
01 FC:1460 130.00 OP

is hereby incorporated by reference therein." A copy of Applicants' Request is attached hereto for the Office's consideration. Thus, even if Applicants failed to include a copy of Figure 1 when the application was filed, Applicants' Request clearly incorporated by reference the disclosure of the prior application, Application Serial No 10/135,763, filed May 1, 2002, which the Patent Office has indicated includes Figure 1. Thus, at least by way of its incorporation by reference of the entire disclosure of '763 application, Applicants submit that the present application included Figure 1 as part of its disclosure at the time it was filed. For the Office's convenience, Applicants also enclose a copy of parent application, as filed, and a copy of the date-stamped postcard from the '763 application, indicating that the Patent Office received a copy of Figure 1 with the '763 application.

In view of Applicants' incorporation by reference of the entire disclosure of the '763 application, which included Figure 1, Applicants submit that the present application is entitled to its April 13, 2004, filing date.

Applicants respectfully request reconsideration and withdraw of the Notice of Incomplete Nonprovisional Application, and a refund of the petition fees of $260.00 (i.e., the $130.00 fee submitted herewith and the $130.00 fee submitted with the Petition filed on August 13) in accordance with 37 C.F.R. § 1.17(h).

Should the Office have any questions concerning this paper or the subject application in general, Applicants invite the Office to telephone the undersigned at its earliest convenience.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: September 30, 2004 By: _____

Martin A. Bruehs
Registration No. 45,635

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Attachments: (1) Applicants' Request For Filing Continuation/Divisional Application Under 37 C.F.R. § 1.53(b)
(2) Date-Stamped Postcard For Application Serial No. 10/135,763, filed May 1, 2002
(3) Copy of Application Serial No. 10/135,763 as filed

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450
www.uspto.gov

JJGJR.: 09-04

Paper No: __

BURNS DOANE
SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA VA 22313-1404

COPY MAILED

SEP 2 1 2004

OFFICE OF PETITIONS

In re Application of
Khanuja, et al.
Application No. 10/822,790
Filing Date: 13 April, 2004
Attorney Docket No. 033166-028

DECISION ON PETITION

This is a decision on the petition filed on 13 August, 2004, to obtain a filing date of 13 April, 2004, for the instant application.

The petition under 37 C.F.R. §1.53 is **DISMISSED**.

BACKGROUND

This nonprovisional application was deposited on 13 April, 2004.

On 7 July, 2004, the Office mailed a "Notice of Incomplete Nonprovisional Application," (the 7 July Notice) and indicated that a filing date had not been granted because the application had been deposited without drawings as required under 35 U.S.C. §113 (first sentence).

The 7 July Notice also informed Petitioner that the application would receive the filing date consistent with the submission of required drawings, or that Petitioner might evidence that either drawings were not necessary for the understanding of the invention or the application as submitted otherwise satisfied the statutory requirements for a filing date.

Petitioner:

- filed the instant petition on 13 August, 2004; and

- alleged that the instant application incorporated by reference the parent such that the presence of the drawing in the parent with the incorporation by reference of that disclosure satisfied the statutory requirement.

When making such an allegation, it is proper to provide a copy of the parent application as filed.

Should Petitioner wish to proceed accordingly with the instant matter, Petitioner should submit a complete copy of the parent application as filed, a copy of the receipt card and a renewed petition. Petitioner should file these materials within two months of the date of this decision.

Further correspondence with respect to this matter should be addressed as follows:

By mail: (Effective 1 May, 2003)[1]
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

By FAX: IFW Formal Filings
(703) 872-9306
(Effective 28 September, 2004: (571-273-0025)
ATTN.: Office of Petitions

By hand: Mail Stop: Petition
Customer Service Window
Lobby/Room 1B03
Crystal Plaza Two
220 20th Street S.
Arlington, VA 22202

Telephone inquiries concerning this decision may be directed to the undersigned at (703)305-9199.

John J. Gillon, Jr.
Senior Attorney
Office of Petitions

[1] To determine the appropriate addresses for other subject-specific correspondence, refer to the USPTO Web site at www.uspto.gov.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

REQUEST FOR FILING CONTINUATION/DIVISIONAL APPLICATION UNDER 37 C.F.R. § 1.53(b)

Mail Stop PATENT APPLICATION
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Customer Number **21839**

Sir:

This is a request for filing a ☐ continuation ☒ divisional application under 37 C.F.R. § 1.53(b) of the following pending application, by the following named inventor(s):

Application No. 10/135,763 Filed: MAY 1, 2002

Title: Use of Bioactive Fraction From Cow Urine Distillate ('Go-Mutra') as a Bio-Enhancer of Anti-Infective, Anti-Cancer Agents and Nutrients

Inventor(s): Suman Preet Singh KHANUJA, Sushil KUMAR, Ajit Kumar SHASANY, Jai Shankar ARYA, Mahendra Pandurang DAROKAR, Monika SINGH, Prachi SINHA, Soumya AWASTHI, Subhash Chandra GUPTA, Vivek Kumar GUPTA, Madam Mohan GUPTA, Ram Kishore VERMA, Sweta AGARWAL, Sunil Balkrishna MANSINGKA and Suresh Haribhau DAWLE

☒ The entire disclosure of the prior application from which a copy of the oath or declaration is supplied herewith is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.

☐ This application is being filed by less than all the inventors named in the prior application. In accordance with 37 C.F.R. § 1.63(d)(2), the Commissioner is requested to delete the name(s) of the following person or persons who are not inventors of the invention being claimed in this application.

☐ This application is being filed by more than all the inventors named in the prior application. In accordance with 37 C.F.R. § 1.63(d)(5), a new oath or declaration is enclosed, and the Commissioner is requested to add the name(s) of the following person or persons who are inventors of the invention being claimed in this application.

DOCKETED
filed 4-13-04

☒ Applicant(s) suggests Figure 1 for inclusion on the front page of the patent application publication and patent.

☒ Applicant(s) requests that the published application include the following assignment information:
COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH
RAFI MARG
NEW DELHI 110 001
INDIA

1. ☒ Enclosed is a copy of the prior Application No. 10/135,763 as originally filed on MAY 1, 2002, including copies of the specification, claims, drawings and the executed oath or declaration as filed.
2. ☐ Enclosed is a revised prior application and a copy of the prior executed oath or declaration as filed. No new matter has been added to the revised application.
3. ☐ Small entity status is hereby claimed.
4. ☒ The filing fee is calculated below ☒ and in accordance with the enclosed preliminary amendment.

CLAIMS

	No. of Claims		Extra Claims	Rate	Fee
Basic Application Fee (1001)					$ 770.00
Total Claims	21	MINUS 20 =	1	x $18.00 (1202) =	$ 18.00
Independent Claims	5	MINUS 3 =	2	x $86.00 (1201) =	$ 172.00
If multiple dependent claims are presented, add $290.00 (1203)					
Total Application Fee					$ 960.00
☐ Small Entity Status claimed - subtract 50% of Total Application Fee					$ 0.00
Add Assignment Recording Fee of $40.00 (8021) if Assignment document is enclosed.					
TOTAL APPLICATION FEE DUE					**$ 960.00**

5. ☐ This application is being filed without a filing fee. Issuance of a Notice to File Missing Parts of Application is respectfully requested.
6. ☐ Charge _____ to Deposit Account No. 02-4800 for the fee due.
7. ☒ A check in the amount of $ 960.00 is enclosed for the fee due.
8. ☐ Charge _____ to credit card. Form PTO-2038 is attached.
9. ☒ The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800. This paper is submitted in duplicate.

10. ☐ Cancel in this application original claims _____ of the prior application before calculating the filing fee.

11. ☐ New drawings are enclosed.

12. ☐ Applicant(s) claims priority under 35 U.S.C. § 119 of the following application(s):

Country	Application No.	Filing Date MM-DD-YYYY

☐ The certified copy of the priority application

☐ is enclosed.

☐ was filed on _____ in prior Application No. _____, filed on _____, and acknowledged by the Examiner on _____ in Paper No. _____.

☐ has not yet been filed.

13. ☒ A preliminary amendment is enclosed.

14. ☐ An Information Disclosure Statement is enclosed.

15. ☐ A General Authorization for Payment of Fees and Petitions for Extensions of Time is enclosed.

16. ☐ Also enclosed is _____

17. ☒ The power of attorney in the prior application is to Norman H. Stepno, Registration No. 22,716 and all partners of Burns, Doane, Swecker & Mathis, L.L.P.

a. ☒ The power appears in the original papers in the prior application.

b. ☐ Since the power does not appear in the original papers, a copy of the power in the prior application is enclosed.

c. ☐ Recognize as Associate Attorney _____

d. ☒ Address all future communications to: (May only be completed by applicant, or attorney or agent of record.)

Burns, Doane, Swecker & Mathis, L.L.P.
Customer Number **2 1 8 3 9**
P.O. Box 1404
Alexandria, Virginia 22313-1404

April 13, 2004
Date

By: Martin A. Bruehs
Martin A. Bruehs
Registration No. 45,635

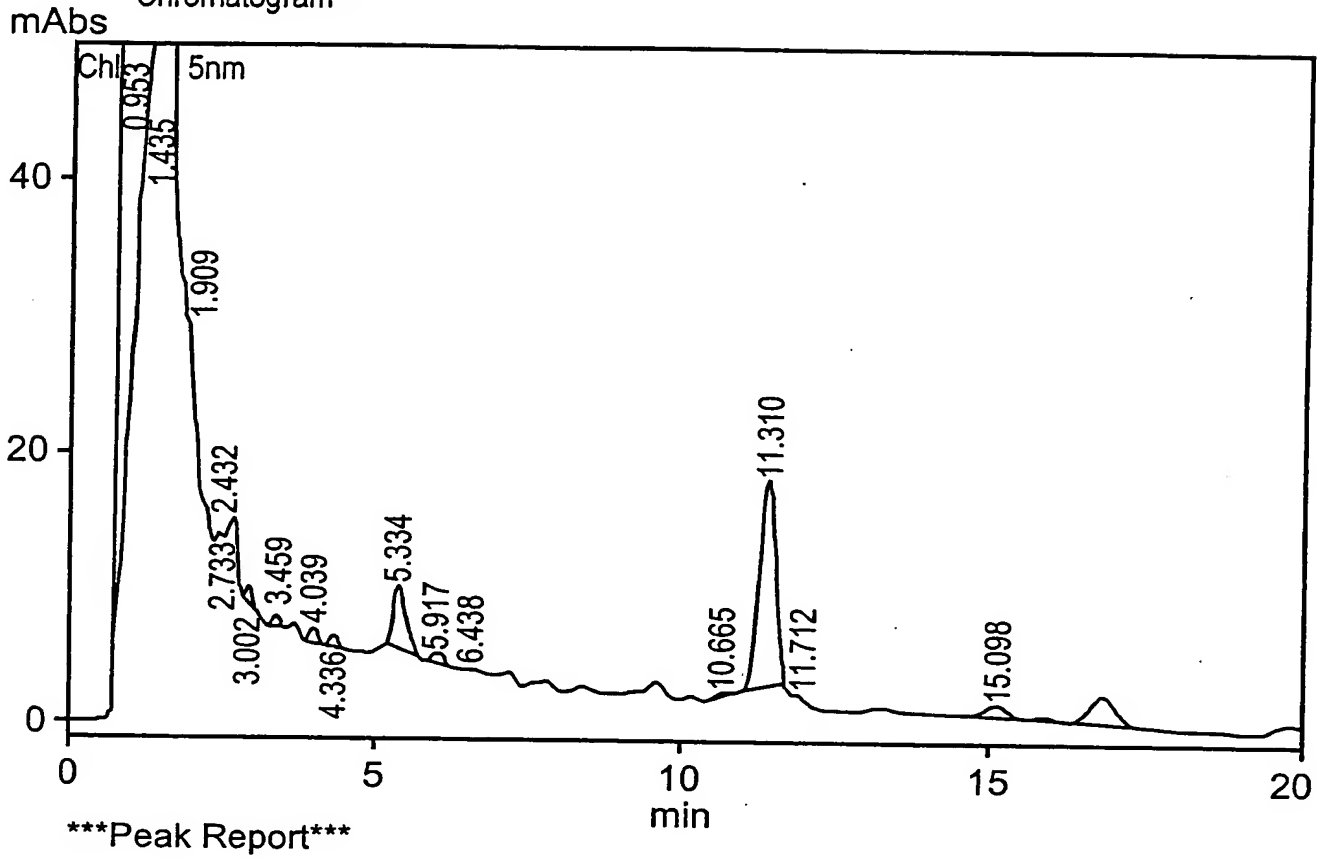
Address of signator:

Burns, Doane, Swecker & Mathis, L.L.P.
P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

☐ inventor(s)
☐ assignee of complete interest
☐ attorney or agent of record
☒ filed under 37 C.F.R. § 1.34(a)

Sample :
ID :
Type : Unknown
Detector : SPD-M10Avp
Operator :
Method Name : ANAL.MET

*** Chromatogram ***



Peak Report

PKNO	ChNO	TIME	AREA	MK	PURITY.UP	PURITY.DOWN	IDNO	CONC
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2	1	1.438	2027186					16.7631
3	1	1.909	7380					0.0610
4	1	2.432	2312					0.0191
5	1	2.733	26772					0.2214
6	1	3.002	11050					0.0914
7	1	3.459	5526					0.0457
8	1	4.039	9699					0.0802
9	1	4.336	9040					0.0748
10	1	5.334	59563					0.4925
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15	1	11.712	2676					0.0221
16	1	15.098	94810					0.7840
			12093144					100.0000

FIG. 1

Inventor: KHANUJA et al. Appln. No. New Divisional Patent Application

Docket No.: 033166-021 Work Atty: NHS:MAB:jjh Date: 5-1-02

Title: PHARMACEUTICAL COMPOSITION CONTAINING COW URINE DISTILLATE AND AN ANTIBIOTIC

The following was/were received in the U.S. Patent and Trademark Office on the date stamped hereon:

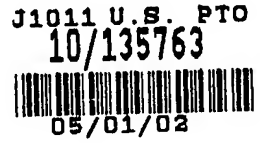
- ☐ Utility Patent Application Transmittal
- ☐ Design Patent Application Transmittal
- ☐ Continuing Prosecution Application Request
- ☐ Provisional Application Cover Sheet
- ☐ Provisional Application Transmittal
- ☒ Continuation/Divisional Application (Rule 53(b)) with copy of application
- ☐ Request for Continued Examination

INCLUDING:

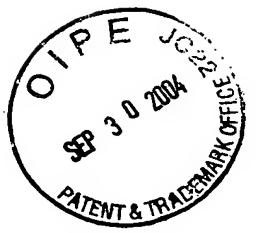
- ☒ Specification (pages 1 - 16)
- ☒ Claims (claim(s) 1 - 35 , 4 pgs.)
- ☒ Drawings (Fig(s). 1 - 1 , 1 pgs.)
- ☒ Abstract of the Disclosure

- ☒ Executed Declaration/Power of Attorney
- ☐ Unexecuted Declaration/Power of Attorney
- ☐ Assignment/Assignment Recordation Form Cover Sheet (PTO-1595)
- ☐ Claim for Convention Priority w/_ certified copy(s)
- ☒ Preliminary Amendment
- ☐ Information Discl. Statement Transmittal Letter
- ☐ Information Disclosure Citation (PTO-1449)
- ☐ Information Disclosure Statement w/_ document(s)
- ☐ Petition for _ Month Extension of Time
- ☐ Constructive Petition for Extensions of Time
- ☐ Patent Application Data Sheet

- ☒ Check for $ 1178.00 is enclosed
- ☐ Check for $__ is enclosed
- ☐ Charge $__ to Deposit Account
- ☐
- ☐
- ☐
- ☐



(11/01)



Patent
Attorney's Docket No. 033166-001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

UTILITY PATENT
APPLICATION TRANSMITTAL LETTER

Box PATENT APPLICATION
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Enclosed for filing is the utility patent application of SUMAN PREET SINGH KHANUJA, SUSHIL KUMAR, AJIT KUMAR SHASANY, JAI SHANKAR ARYA, MAHENDRA PANDURANG DAROKAR, MONIKA SINGH, PRACHI SINHA, SOUMYA AWASTHI, SUBHASH CHANDRA GUPTA, VIVEK KUMAR GUPTA, MADAN MOHAN GUPTA, RAM KISHORE VERMA, SWETA AGARWAL, SUNIL BALKRISHNA MANSINGHKA, and SURESH HARIBHAU DAWLE for "USE OF BIOACTIVE FRACTION FROM COW URINE DISTILLATE ("GO-MUTRA") ASA BIO-ENHANCER OF ANTI-INFECTIVE, ANTI-CANCER AGENTS AND NUTRIENTS".

[ ] Applicant(s) hereby request(s) that the above-captioned application **NOT BE PUBLISHED** under 35 U.S.C. § 122(b) and 37 C.F.R. § 1.211. The undersigned hereby certifies that the invention disclosed in this application has not and will not be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

[X] Applicant(s) suggest(s) Figure 1 for inclusion on the front page of the patent application publication and patent.

Also enclosed are:

[X] 1 sheet(s) of [ ] formal [X] informal drawing(s);

[ ] a claim for foreign priority under 35 U.S.C. §§ 119 and/or 365 is [ ] hereby made to _ filed in _ on _;

[ ] in the declaration;

[ ] a certified copy of the priority document;

[ ] a General Authorization for Petitions for Extensions of Time and Payment of Fees;

[ ] an Assignment document;

[ ] an Information Disclosure Statement;

[ ] a bibliographic data entry sheet; and

[X] Other: Preliminary Amendment.

21839

DOCKETED
filed 12/1/00

(11/00)

[X] An [ ] executed [X] unexecuted declaration of the inventor(s)

[X] also is enclosed [ ] will follow.

[X] Please amend the specification by inserting before the first line the sentence --This application claims priority under 35 U.S.C. §§ 119 and/or 365 to 60/241,842 filed in the United States on October 20, 2000; the entire content of which is hereby incorporated by reference.--

[ ] Please amend the specification by inserting before the first line the sentence --This application is a continuation of International Application No. _ filed on _, which designates the United States.--

[ ] Small entity status is hereby claimed.

[X] The filing fee has been calculated as follows [X] and in accordance with the enclosed preliminary amendment:

CLAIMS					
	NO. OF CLAIMS		EXTRA CLAIMS	RATE	FEE
Basic Application Fee					$710.00 (101)
Total Claims	35	MINUS 20 =	15	× $18.00 (103) =	$270.00
Independent Claims	5	MINUS 3 =	2	× $80.00 (102) =	$160.00
If multiple dependent claims are presented, add $270.00 (104)					
Total Application Fee					$1,140.00
If small entity status is claimed, subtract 50% of Total Application Fee					
Add Assignment Recording Fee $ if Assignment document is enclosed					
TOTAL APPLICATION FEE DUE					$1,140.00

[ ] This application is being filed without a filing fee. Issuance of a Notice to File Missing Parts of Application is respectfully requested.

[X] A check in the amount of $ 1,140.00 is enclosed for the fee due.

[ ] Charge $ _____ to Deposit Account No. 02-4800 for the fee due.

[X] The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800. This paper is submitted in duplicate.

Please address all correspondence concerning the present application to:

Norman H. Stepno, Esquire
BURNS, DOANE, SWECKER & MATHIS, L.L.P.
P.O. Box 1404
Alexandria, Virginia 22313-1404.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: December 1, 2000

By: _____
Norman H. Stepno
Registration No. 22,716

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (Includes Reference to Provisional and PCT International Applications)	Attorney's Docket No. 033166-001

As a below named inventor, I hereby declare that:
My residence, post office address and citizenship are as stated below next to my name;
I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

USE OF BIOACTIVE FRACTION FROM COW URINE DISTILLATE ("GO-MUTRA") AS A BIO-ENHANCER OF ANTI-INFECTIVE, ANTI-CANCER AGENTS AND NUTRIENTS

the specification of which (check only one item below):

☒ is attached hereto.

☐ was filed as United States application
Number _____
on _____
and was amended
on _____ (if applicable).

☐ was filed as PCT international application
Number _____
on _____
and was amended
on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 (a)-(e) of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. §119:

COUNTRY (if PCT, indicate "PCT")	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 U.S.C. §119
			_ Yes _ No
			_ Yes _ No
			_ Yes _ No
			_ Yes _ No
			_ Yes _ No

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below.

60/241,842	October 20, 2000
(Application Number)	(Filing Date)
(Application Number)	(Filing Date)

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (CONT'D) (Includes Reference to Provisional and PCT International Applications)	Attorney's Docket No. 033166-001

I hereby claim the benefit under Title 35, United States Code, §120 of any United States applications(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose to the Office all information known to me to be material to the patentability as defined in Title 37, Code of Federal Regulations §1.56, which became available between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 U.S.C. §120:

U.S. APPLICATIONS		STATUS *(check one)*		
U.S. APPLICATION NUMBER	U.S. FILING DATE	PATENTED	PENDING	ABANDONED

PCT APPLICATIONS DESIGNATING THE U.S.					
PCT APPLICATION NO.	PCT FILING DATE	U.S. APPLICATION NUMBERS ASSIGNED (if any)			

I hereby appoint the following attorneys and agent(s) to prosecute said application and to transact all business in the Patent and Trademark Office connected therewith and to file, prosecute and to transact all business in connection with international applications directed to said invention:

William L. Mathis	17,337	R. Danny Huntington	27,903	Gerald F. Swiss	30,113
Robert S. Swecker	19,885	Eric H. Weisblatt	30,505	Charles F. Wieland III	33,096
Platon N. Mandros	22,124	James W. Peterson	26,057	Bruce T. Wieder	33,815
Benton S. Duffett, Jr.	22,030	Teresa Stanek Rea	30,427	Todd R. Walters	34,040
Norman H. Stepno	22,716	Robert E. Krebs	25,885	Ronni S. Jillions	31,979
Ronald L. Grudziecki	24,970	William C. Rowland	30,888	Harold R. Brown III	36,341
Frederick G. Michaud, Jr.	26,003	T. Gene Dillahunty	25,423	Allen R. Baum	36,086
Alan E. Kopecki	25,813	Patrick C. Keane	32,858	Steven M. duBois	35,023
Regis E. Slutter	26,999	B. Jefferson Boggs, Jr.	32,344	Brian P. O'Shaughnessy	32,747
Samuel C. Miller, III	27,360	William H. Benz	25,952	Kenneth B. Leffler	36,075
Robert G. Mukai	28,531	Peter K. Skiff	31,917	Fred W. Hathaway	32,236
George A. Hovanec, Jr.	28,223	Richard J. McGrath	29,195		
James A. LaBarre	28,632	Matthew L. Schneider	32,814		
E. Joseph Gess	28,510	Michael G. Savage	32,596		

21839

and: _____

Address all correspondence to:

21839

Norman H. Stepno, Esquire
BURNS, DOANE, SWECKER & MATHIS, L.L.P.
P.O. Box 1404
Alexandria, Virginia 22313-1404

Address all telephone calls to: Norman H. Stepno at (703) 836-6620.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (CONT'D) (Includes Reference to Provisional and PCT International Applications)	Attorney's Docket No. 033166-001

FULL NAME OF SOLE OR FIRST INVENTOR	SIGNATURE	DATE
SUMAN PREET SINGH KHANUJA		
RESIDENCE	CITIZENSHIP	
LUCKNOW 226 015 (UP), INDIA	INDIA	
POST OFFICE ADDRESS		
Central Institute of Medicinal and Aromatic Plants, P.O. CIMAP, Lucknow 226 015 (UP), India		
FULL NAME OF SECOND JOINT INVENTOR, IF ANY	SIGNATURE	DATE
SUSHIL KUMAR		
RESIDENCE	CITIZENSHIP	
LUCKNOW 226 015 (UP), INDIA	INDIA	
POST OFFICE ADDRESS		
Central Institute of Medicinal and Aromatic Plants, P.O. CIMAP, Lucknow 226 015 (UP), India		
FULL NAME OF THIRD JOINT INVENTOR, IF ANY	SIGNATURE	DATE
AJIT KUMAR SHASANY		
RESIDENCE	CITIZENSHIP	
LUCKNOW 226 015 (UP), INDIA	INDIA	
POST OFFICE ADDRESS		
Central Institute of Medicinal and Aromatic Plants, P.O. CIMAP, Lucknow 226 015 (UP), India		
FULL NAME OF FOURTH JOINT INVENTOR, IF ANY	SIGNATURE	DATE
JAI SHANKAR ARYA		
RESIDENCE	CITIZENSHIP	
LUCKNOW 226 015 (UP), INDIA	INDIA	
POST OFFICE ADDRESS		
Central Institute of Medicinal and Aromatic Plants, P.O. CIMAP, Lucknow 226 015 (UP), India		
FULL NAME OF FIFTH JOINT INVENTOR, IF ANY	SIGNATURE	DATE
MAHENDRA PANDURANG DAROKAR		
RESIDENCE	CITIZENSHIP	
LUCKNOW 226 015 (UP), INDIA	INDIA	
POST OFFICE ADDRESS		
Central Institute of Medicinal and Aromatic Plants, P.O. CIMAP, Lucknow 226 015 (UP), India		
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COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (CONT'D) (Includes Reference to Provisional and PCT International Applications)	Attorney's Docket No. 033166-001

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Patent
Attorney's Docket No. 033166-001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	
	)	
Suman Preet Singh KHANUJA et al.	)	Group Art Unit: Unassigned
	)	
Application No.: Unassigned	)	Examiner: Unassigned
	)	
Filed: December 1, 2000	)	
	)	
For: USE OF BIOACTIVE FRACTION FROM COW URINE DISTILLATE ("GO-MUTRA") AS A BIO-ENHANCER OF ANTI-INFECTIVE, ANTI-CANCER AGENTS AND NUTRIENTS	)	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In advance of the initial Official Action on the substantive merits thereof, please preliminarily amend the application identified in caption as follows:

IN THE CLAIMS:

Claim 35, line 1, please change "claims 1-34" to --claim 1--.

REMARKS

Entry of the foregoing amendment is respectfully requested; it simply avoids

multiple claim dependency.

Respectfully submitted,

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USE OF BIOACTIVE FRACTION FROM COW URINE DISTILLATE *('GO-MUTRA')* AS A BIO-ENHANCER OF ANTI-INFECTIVE, ANTI-CANCER AGENTS AND NUTRIENTS

Field of the Invention

The invention relates to an absolutely novel use of cow urine distillate as activity enhancer and availability facilitator for bioactive molecules including anti-infective and anti-cancer agents. The molecules which express any activity in form of either inhibiting or promoting a biological function have been referred in this invention as bioactive molecule e.g. antibiotics, drugs, nutraceuticals, cardiovascular, hepatoprotective, neuro-tonics *etc.* The present invention has direct implication in drastically reducing the dosage of antibiotics, drugs and anti-cancer agent while increasing the efficiency of absorption of bioactive molecules.

Background of the invention

In Ayurveda cows urine is suggested for improving general health. But it is never scientifically tested for any utility alone. The applicants have developed the curiosity about this component in the preparations and asked many questions to them; whether the component cow urine is having any activity by itself or it does not have any activity but enhance the activity of other components in the preparations? What are the components present in the urine of cow? Whether the urine contains microorganism, which are beneficial? Whether the degradation products from the urine are beneficial? To answer these questions the applicant obtained "Kamadhenu Arka" the urine distillate from "Go-Vigyana Anusandhana Kendra" Nagpur, India. This is the urine distillate suggested for drinking to improve the general health and sold and distributed in different size bottles. The applicants tested the urine on Luria agar and broth in sterile condition and did not notice any growth of microorganism. To test whether this is inhibitory to growth of different microorganism, *Escherichia coli* and *Mycobacterium smegmatis* were grown at different temperatures ranging from 20 to 40°C in presence and in absence of the cow urine distillate, no significant difference in the colony count is noticed. Surprisingly, the same distillate enhanced the antibiotic action on these bacteria leading to this invention. The novelty of the invention lies in the fact revealed through precise experimentation that the

enhancement action and its effectiveness is achievable only in the range of concentration which is literally in nano to micro molar levels. And when a higher concentration / dosage is used in the formulation or combinations the activity(ies) do not appear. That should be the reason for non-detection such a valuable potential of cow urine (*Go-mutra)*. From million doses of annual antibiotics consumption goes waste as these could not be utilized or targeted to the infective organisms effectively due to various factors like efficient absorption, transportation to the target site, retention time, operation of efflux pump, metabolism *etc.* Thus, large portions of the drugs we apply are wasted and only a miniscule percentage is being targeted to the infective microbes. Also, the unutilized drug / antibiotic amount remains as a load in the body and environment acting as a selection pressure to facilitate emergence of drug resistance in parasites and their predominance, ultimately leading to failure of antibiotics against resistant infections. This also is responsible for side effects, illness and reduction in life expectancy being more acute in the older population. One of the ways, which has been feasible to reduce drug dosage, has been synergism between two therapeutic agents. However, if both have the antibiotic property, still the problem of continued selection pressure on microbes is likely to continue. So, the applicants thought of utilizing cow urine, which is not microbicidal but when present with a drug or active molecule, enhance its activity and availability (bioenhancers). This way, the selection pressure will be counter-balanced simultaneously reducing the dosage of antibiotics or drugs for minimizing the side effects, which has also high commercial importance.

The present invention was the result of planned experiments to provide a novel method for improving activity and bioavailability of antibiotics, drugs and other molecules using 'cow urine distillate' in different formulations.

The bioavailability of nutrients and enhancement antibiotics effect is relevant to human, plant as well as animal health and thus the compositions and methods of the invention are also intended to be used in agriculture and veterinary practice.

Description of related Art

Cow's urine (*Go-mutra*) can be considered as the most effective animal origin substance/secretion with the capacity of general health improvement but it does need substantiation through scientific experimentation. Thus, the applicants considered it worthwhile to scientifically look at this and define the molecular basis of the values through *in vitro* and *in vivo* assays. The applicants in the first instance probed whether it contained any drug facilitator elements since such a property would make it a highly useful natural substance. In recent days, use of 'piperine' as a bioavailability enhancer has been described (United States Patents 5,616,593 and 5,972,382). Till today thus, the known bioavailability enhancer documented is piperine and a series of inventions related to this compound have been described in the following prior arts.

Objects of the invention.

The main objective is to provide new use of the bio- active fraction as a bio-enhancer and as a bioavailability facilitator.

In another objective of the invention is to provide method for improving activity and bioavailability of antibiotics, drugs and other molecules using active fraction from cow urine distillate.

Still another objective of the invention is to provide a process for the extraction of the active fraction form the cow urine.

Summary of the invention

The invention relates to new use of a known abundantly available cow urine distillate as an enhancer of antibiotic action on the target. The molecule of invention helps in the absorption of antibiotics across the cell membrane in animal cells, gram positive and gram negative bacteria. Similar activities can also be obtained by using the distillate of the urine of cow at 40–50°C and from the concentrate, which is lyophilized and dissolved for further use. Further the urine distillate from buffalo, camel, deer provides similar activity of bioavailability.

Brief description of the accompanying drawing

Fig.1 represents HPLC characters of cow urine (*Go-mutra*) distillate

Detailed description of the invention

Our emphasis here was to search a plentifully available material with bioenhancing action of higher potency. Additionally, a property that the applicants searched was the bioenhancement of a scarcely available anti-cancer natural agent 'taxol' (peclitaxel) which is produced in microscopic amounts by the Yew tree (*Taxus* spps.) and hence is always a limited molecule in availability. Cow urine distillate enhanced the killing activities of different antibiotics on bacteria. More important was the obvious enhancement in the cell division inhibitory activity against the breast cancer cell line MCF-7.

In an embodiment of the present invention a pharmaceutical composition comprising an effective amount of cow urine distillate as a bioavailability facilitator and a pharmaceutically acceptable additives selected from anticancer compounds, antibiotics, drugs, therapeutic and nutraceutic agents, ions and similar molecules which are targeted to the living systems.

In another embodiment, the cow urine distillate is used as bioavailability facilitator for anticancer therapy directly or in combination with anticancer molecules.

In still another embodiment, the cow urine distillate is used in antifungal therapy for fungal infections.

In yet another embodiment, the antifungals are azoles, clotrimazole, mystatin, amphotericin and similar materials.

In yet another embodiment, fungi covering infections are mycetial, candida, yeast or other fungicidal compounds.

In still another embodiment, the cow urine distillate is used in TB therapy including multi drug resistant tuberculosis in combination with isoniazid and other anti-tubercular agents.

In yet another embodiment, the bioavailability facilitator helps in transferring the compound across the membrane and for better effectivity on the target site.
In yet another embodiment, the antibiotics are Quinolones, fluoroquinolones like Nalidixic acid and others like Rifampicin, Tetracycline, ampicillin and similar compounds.

In yet another embodiment, the antibiotics, ions and similar compounds are isoniazid and hydrogen peroxide.

In yet another embodiment, the bioavailability facilitator helps the antibiotics and other molecules to act better on the target by increasing the effectivity.

In yet another embodiment, the living system may be bacteria, fungi or any living cells.

In yet another embodiment, the anti bacterial agents are selected from the group comprising Quinolones, Rifampicin, Tetracycline and ampicillin.

In yet another embodiment, the cow urine (*Go-mutra*) distillate is in the range between 0.001 µl/ml to 100 µl/ml.

In yet another embodiment, the lyophilized active fraction used is in the range between 0.1 µg/ml to 100 µg/ml.

In still another embodiment, the bioactive fraction enhances the activity of anti-bacterial agents, anti-cancer agents and anti-tuberculosis agents from 2 to 80 folds.

In yet another embodiment, the bioactive fraction enhances the activity of anti-bacterial agents from 2 to 80 folds.

In yet another embodiment, the anti bacterial agent is an anti-tuberculosis agent selected from isoniazid, pyrazinamide and other similar compounds.

In yet another preferred embodiment, the bioactive fraction enhances the activity of anti-tuberculosis agents from 2 to 20 folds.

In yet another embodiment of the invention, the anti-cancer agent is selected from group consisting of Paclitaxel (Taxol).

In yet another preferred embodiment of the invention, the bioactive fraction enhances the activity of anti-cancer agents from 2 to 20 folds.

The methodology followed by us for this screening included specifically designed bioassays as described below. The bacterial and fungal strains used in this invention were acquired commercially from Institute of Microbial Technology (IMTECH), Chandigarh which possessed corresponding properties of the ATCC strain mentioned.

1. Assay for bio-enhancement of anti-infective agents

a) The minimum inhibitory concentration (MIC) of antibiotic is determined against *Escherichia coli* (equivalent of ATCC 10536), *Bacillus subtilis* (equivalent of ATCC 6015) and *Mycobacterium smegmatis* (equivalent of ATCC 10231) in broth and disc diffusion assay.

b) The antibiotics agents at concentrations 1/4, 1/3, 1/2 and equal to MIC are added alone and in combination with the test compound at varying concentrations on disc and in broth to evaluate the comparative inhibition.

c) These combination showing significant advantage or higher activity than antibiotic alone in terms of enhanced inhibition of bacterial growth (large inhibition zone in disc diffusion and affectivity of lower concentration in broth assay) are picked up for future testing.

d) In broth assay the activity is quantified by counting number of viable cells in a given treatment and converted in fold enhancement by combination compared to antibiotic / drug alone in the killing percentage of cells.

e) The pre-treatment assay followed to determine whether the compound is required along with antibiotic to enhance its activity or even its withdrawal after treatment or prior to antibiotic treatment would benefit. For this, the cells are treated with compound for 4 to 8 hours and then washed free of it by centrifugation and washing in sterile water. This was followed by treatment with antibiotic as in steps b to d.

2. Assay for bio-enhancement of anti-cancer agents

a) MCF-7 (Breast cancer commercial cell line obtained from National Center for Cell Sciences (NCCS), Pune) is inoculated at a density of about 0.1 X 10^6 cells in MEM medium in the wells of 24 well plate.

b) This is replaced with fresh medium after 18 hours in each well.

c) The test component (s) is added at desired concentrations in different wells just after the medium replacement.

d) Observations are recorded on the cell count after 36 hours for which the following steps are required.

i. The medium is removed from the wells.

ii. The wells are rinsed with 1ml PBS (Phosphate buffer saline).

iii. To each well 500 µl of freshly prepared trypsin (0.1% in PBS) solution is added.

iv. Trypsin solution is removed after 30 seconds and the plate is gently tapped till the cells are released from the plate surface.

v. Fresh 1 ml of MEM growth medium is added and agitated with a pipette to obtain a cell suspension.

vi. 10 µl of cell suspension is taken on the haemocytometer and a cover glass is placed over the counting chamber.

vii. The number of viable cells is counted in 5 big squares and the readings are taken from 5 microscopic fields to determine the average.

viii. The cell count (titer per ml) in the original sample is then calculated as average count X 10^3.

Composition of Minimum Essential Medium (MEM): 100 ml

MEM powder (Sigma –Aldrich, USA)	=	0.96 g
HEPES Buffer (Sigma –Aldrich, USA)	=	0.26 g
Sodium Bicarbonate	=	0.22 g
Penicillin G	=	10 mg
Streptomycin	=	20 mg
Gentamycin	=	5 mg

Foetal Calf Serum	=	15 ml
Foetal Calf Serum	=	15 ml
Distilled water	=	85 ml

3. Bioavailability tests through biological membrane

a) Specially designed U-tubes of glass consisting of two components (opposite-L type) were used in which one open end of an L-shaped was tapered to fit within the untapered end of the other L-tube (Fig 1).

b) The membrane of goat gut (initial part) was stretched and fixed to act as the barrier between the two ends such that by joining the two L-tubes, a U-tube was made.

c) Sterile distilled water was then filled in both the sides to equal height/level.
The antibiotic/compound was added to the donor tube (tapered) and through spectrophotometer, the transfer of molecule was observed using UV and visible absorption maxima of the respective molecules by taking the OD at defined wavelengths.

Examples

In the next step of elucidation of the enhancer action, the applicants experimented with the killing activities of different antibiotics against the bacteria singly and in combination with the test component (cow urine distillate) following the method described above. These experiments are being described in the following examples. When the bacteria were grown in presence of the compound as such no significant killing was observed. In all the experiments the cow urine distillate concentration was kept at 1 µl/ml, unless it is specifically mentioned.

Example 1. Cow urine distillate mediated enhancement in the killing action of antibiotics against Gram-negative bacterium *Escherichia coli*.

Table 1:

Antibiotics	Concentration µg/ml	Survival fraction of viable cells upon treatment with antibiotic alone	Survival fraction of viable cells upon treatment with antibiotic + cow urine distillate combination	* Fold enhancement in antibiotic activity
Rifampicin	10	0.86	0.17	5.0
Rifampicin	30	0.05	0.007	7.1
Ampicillin	4	1.11	0.60	1.85
Ampicillin	6	0.09	0.02	4.50
Ampicillin	8	0.05	0.01	5.00

It was calculated as Survival fraction of viable cells upon treatment with antibiotic and cow urine distillate in combination / Survival fraction of viable cells upon treatment with antibiotic alone

Example 2. Cow urine distillate mediated enhancement in the killing action of antibiotics against Gram-positive bacterium *Bacillus subtilis*.

Table 2:

Antibiotics	Concentration µg/ml	Survival fraction of viable cells upon treatment with antibiotic alone	Survival fraction of viable cells upon treatment with antibiotic + cow urine distillate combination	* Fold enhancement in antibiotic activity
Rifampicin	0.005	1.1	0.28	5.5
Rifampicin	0.05	0.03	0.01	3.0
Ampicillin	0.1	1.00	0.3	3.3
Ampicillin	0.5	0.18	0.06	3.0

Example 3. Cow urine *(Go-mutra)* distillate mediated enhancement in the killing action of antibiotics against bacterium *Mycobacterium smegmatis*

Table 3:

Antibiotics	Concentration µg/ml	Survival fraction of viable cells upon treatment with antibiotic alone	Survival fraction of viable cells upon treatment with antibiotic + cow urine distillate combination	* Fold enhancement in antibiotic activity
Rifampicin	0.05	0.008	0.0001	80
Rifampicin	0.1	0.006	0.0036	1.5
Ampicillin	0.5	0.07	0.006	11.6

Example 4: Cow urine distillate mediated enhancement in the killing action of izoniazid and hydrogen peroxide against *oxyR* mutant of bacterium *Escherichia coli*. The cow urine distillate concentration is 0.001 µl/ml

Table 4:

	Concentration	Survival fraction of viable cells upon treatment with isoniazid/H_2O_2 alone	Survival fraction of viable cells upon treatment with a isoniazid/H_2O_2 + cow urine distillate combination	Fold enhancement in isoniazid/H_2O_2 activity
Isoniazid	250µg/ml	7.5×10^7	0.99×10^7	7.5
Hydrogen peroxide (H_2O_2)	0.003 % v/v	7.14×10^7	1.2×10^7	5.9

The *oxyR* gene is required for the induction of a regulon of hydrogen peroxide-inducible genes in *Escherichia coli* (Christman M F, Storz G and Ames BN (1989) Oxy R, a positive regulator of hydrogen peroxide-inducible genes in *Escherichia coli* and *Salmonella typhimurium*, is homologous to a family of bacterial regulatory proteins (Proc. Natl. Acad. Sci. (USA). 86:3484-3488.). The mutants of these genes are sensitive to drugs like isoniazid and hydrogen peroxide, which produce free radicals, damaging the cellular systems. So the killing activities of these compounds are increased by 5 to 8 folds by cow urine.

Example 5: Cow urine distillate mediated enhancement in the activity of anti cancerous compounds. The cow urine distillate concentration is 1 µl/ml

Table 5:

Taxol Concentration µg/ml	Initial titre of viable cells	Final titre of viable cells upon treatment with taxol alone	Final titre of viable cells upon treatment with taxol + cow urine distillate
0.001	0.9×10^{-6}	0.059×10^6	0.039×10^6
0.005	0.9×10^{-6}	0.042×10^6	0.032×10^6
0.01	0.9×10^{-6}	0.036×10^6	0.012×10^6

The applicants observed similar results of enhancement in the animal cell culture (cancerous cell line MCF-7 obtained from National Center for Cell Sciences (NCCS), Pune), in which the killing action of anti cancerous chemical 'Taxol' is increased. The components of cow urine distillate in our study help in transferring other compounds across the membrane thereby increasing the absorption in, irrespective of bacteria, animal and plant cell. This in-turn has immense importance for absorption of the drugs, pharmaceuticals, nutraceutical and other related compounds and ions by the cells.

Example 6: Bioenhancement of antifungal agent clotrimazol by bioactive Fraction Gm-IV. The concentration of the active fraction is kept at 10 μg/ml.

Table 6

Treatment	Minimum inhibitory Concentration (MIC) in μg/ml	Fold enhancement
Clotrimazol	4.40	0.0
Clotrimazol + Gm IV	0.88	5.0

In other observations the compound cow urine distillate enhances the transport of antibiotics e.g. Rifampicin, Tetracycline, Ampicillin across the gut as well as artificial membrane. The enhancement in transport is approximately 2 to 7 folds.

Great emphasis now is being laid towards quality assurance of crude drugs from alternative sources widely used in the Indian system of medicine. The present invention enlarges the scope and use of the cow urine distillate in therapeutical and nutraceutical application.

Example 7

Development of powder form: For enhancing the utility and convenience of application of cow urine (*Go-mutra*), the applicants further fractionated to reach a solid form which is also free of the typical smell of cow urine distillate that it is more readily acceptable to the humans. For this purpose the urine distillate was fractionated as described by the following procedure:

Fractionation of a white crystalline solid from cow urine.

Step 1: Cow urine is collected aseptically in the stainless steel container directly from the cow, which is maintained in hygienic environment

Step 2: Fifteen liters of cow urine is distilled continuously at 40 – 50 °C in glass distillation apparatus to obtain 10 – 12 liters of the distillate in 16 to 18 hours.

Step 3: The distillate is packed in surface sterilized plastic or glass container for further use

Step 4: 200 ml of cow urine distillate was mixed with half the volume of methanol and extracted with hexane.

Step 5: The hexane fraction (Gm-I) was lyophilized and tested for similar activity as that of cow urine (*Go-mutra*).

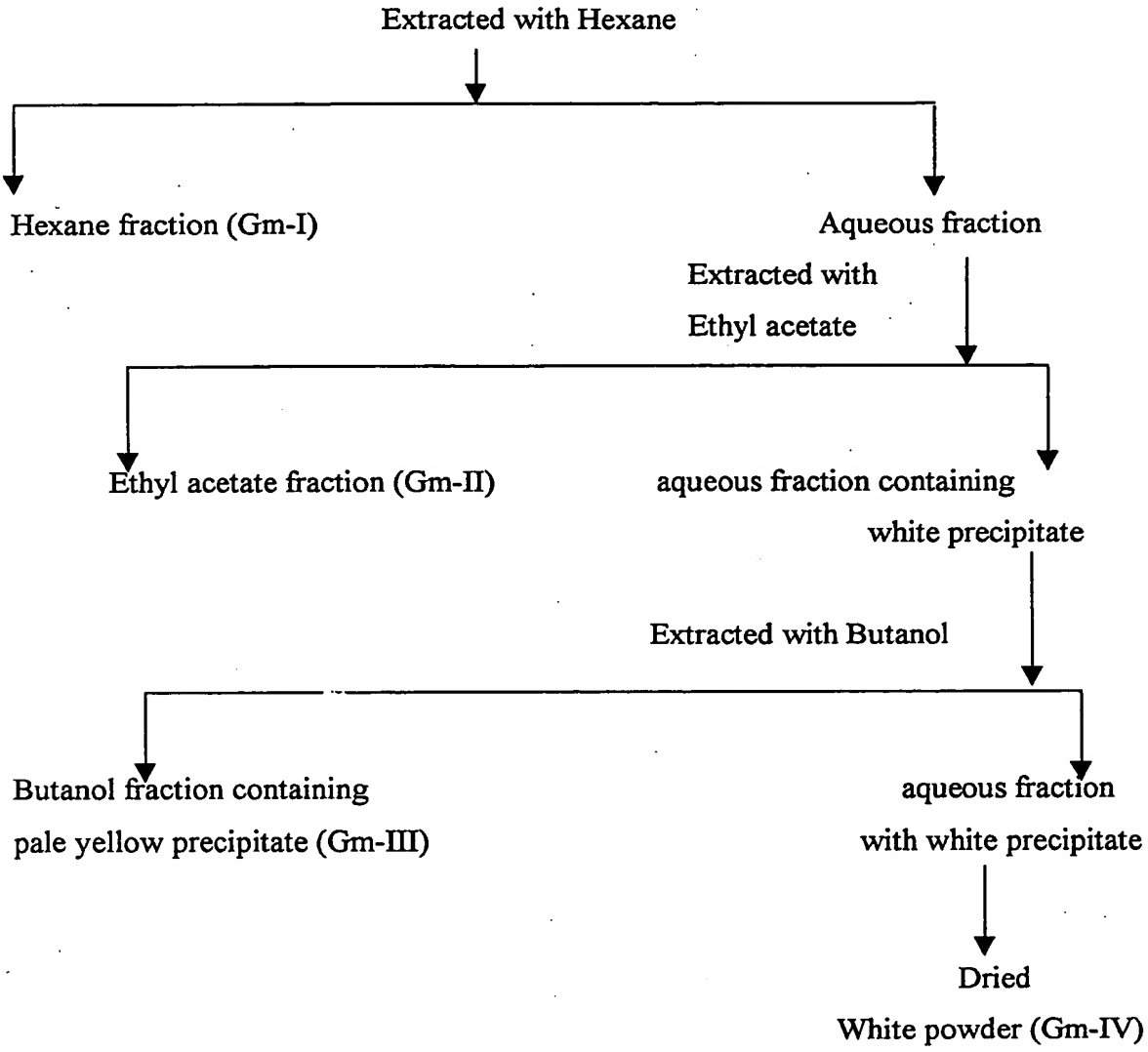
Step 6: The aqueous fraction was extracted with ethyl acetate and the ethyl acetate fraction (Gm-II) was lyophilized and tested for similar activity as that of cow urine (*Go-mutra*).

Step 7: Further, aqueous fraction containing white precipitate was extracted with butanol and the butanol fraction (Gm-III) having pale yellow precipitate was lyophilized and tested for similar activity as that of cow urine (*Go-mutra*).

Step 8: The remaining aqueous fraction containing white crystalline precipitate (Gm-IV) was dried and tested for similar activity as that of cow urine (*Go-mutra*).

Scheme

200 ml cow urine distillate mixed with 100 ml methanol



The white powder (Gm-IV) that was obtained in the range of 10 to 20 grams per 100 ml of the distillate showed all the above activities as described for cow urine distillate at concentration 0.001 to 10 μg/ml, with much more stability and being devoid of the unpleasant smell and hence was used as the advanced product of the invention. The novelty of the invention lies in the fact revealed through precise experimentation that the enhancement action and its effectiveness is achievable only in the range of concentration which is literally in nano to micro molar levels. And when a higher concentration / dosage is used in the formulation or combinations the activity(ies) do not appear.

Physical characters of the Gm-IV fraction

Color: White

Physical state: Solid Crystalline

Solubility: Water-soluble and mixture containing water

Melting point: Above 400°C

Specific Gravity: 1.006

RF value in methanol: Chloroform (50: 50) phase: 0.65

HPLC Characterization of cow urine (*Go-mutra*) distillate

HPLC was performed on LC-8A Shimadzu HPLC with mobile phase water: acetonitrile (80:20), flow rate 1.0ml/min, UV detection at 275 nm and C-18 E MERCK (150 X 4 mm) column. Two major peaks (retention time 5.334 and 11.310 min) observed in the profile of cow urine (*Go-mutra*) distillate (Figure 1).

Further characterization to test the chemical nature of the compound was performed through Feigl's test (In: E Stahl, Thin Layer Chromatography) which was positive indicating the presence of glycoside or sugar.

The novelty of the invention is that from cow urine (*Go-mutra*) distillate, a stable solid fraction could be isolated which is water soluble and devoid of the urine smell and can directly be used in any formulation.

The fraction Gm-IV also enhances the transport of antibiotics and vitamins across the mammalian gut membrane. The example describing the enhanced transport of rifampicin by the fraction Gm-IV is given below.

Example 8: Fraction Gm-IV of cow urine (*Go-mutra*) distillate mediated enhancement in the bioavailability across the biological membrane (Rifampicin, 1mg/ml and fraction Gm-IV, 1.0μg/ml).

Table 7:

Compound(s) in the donor tube	Wave length (nm)	OD measured as Absorbance (specific to the compound maxima) across the membrane in receiving tube after					
		1 hr	2 hr	3 hr	4hr	5 hr	6 hr
Rifampicin	A_{340}	0.0097	0.0214	0.0334	0.0771	0.0858	0.0910
	A_{475}	0.0177	0.0284	0.0309	0.0412	0.0484	0.0496
Rifampicin + Gm-IV	A_{340}	0.0525	0.0961	0.1353	0.1639	0.1919	0.1989
	A_{475}	0.0502	0.0904	0.0793	0.0966	0.1157	0.1183

As cow urine (*Go-mutra*) distillate and the fraction Gm-IV, both shows enhanced membrane permeability by enhancing the antibiotics across the semi-permeable membrane and mammalian gut membrane, it can be assumed the above substances can be used for enhancing intestinal transport and transport of molecules across membranes of various biological functions including urinary / renal systems.

In all the experiments 1 to 5, the enhancing activity of the lyophilized product of the invention is found to have same enhancing activity like that of the distillate.

The invention can further be explained as follows:

1. The sample shows enhancement of bioavailability of rifampicin (antibiotic) and Vitamin B-12 across the mammalian gut membrane (Goat intestine was used) within 2 hours and it keeps increasing upto 4 hours.
2. It shows clear inhibition of ascorbic acid action to prevent oxidation of cut apple indicating that it probably enhances the isoniazid (INH) by oxidative mechanism that synergises the drug action of INH.
3. The distillate showed enhancement action for INH even at 10-50 thousand-fold dilution in the final volume of culture.

4. Still more interesting observation is that at 1 µl/ml the distillate showed enhancement in the activity of taxol by at least 5 folds. Further experiments in this direction have been taken up on priority.

Claims

1. A pharmaceutical composition comprising an effective amount of cow urine distillate as a bioavailability facilitator and pharmaceutically acceptable additives selected from anticancer compounds, antibiotics, drugs, therapeutic and nutraceutic agents, ions and similar molecules which are targeted to the living systems.
2. A composition as claimed in claim 1 wherein, the cow urine distillate is used as bioavailability facilitator for anticancer therapy directly or in combination with anticancer molecules.
3. A composition as claimed in claim 1 wherein, the cow urine distillate is used in TB therapy including multi drug resistant tuberculosis in combination with isoniazid and other anti-tubercular agents.
4. A composition as claimed in claim 1 wherein, the cow urine distillate is used in antifungal therapy for fungal infections.
5. A composition as claimed in claim 1 wherein, the bioavailability facilitator helps in transferring the compound across the membrane and for better effectivity on the target site.
6. A composition as claimed in claim 1 wherein, the antibiotics are but not limited to fluoroquinolones like Nalidixic acid and others like Rifampicin, Tetracycline, amphilicin and similar compounds.
7. A composition as claimed in claim 1 wherein, the antibiotics, ions and similar compounds are isoniazid and hydrogen peroxide.
8. A composition as claimed in claim 1 wherein, the bioavailability facilitator helps the antibiotics and other molecules to act better on the target by increasing the effectivity.
9. A composition as claimed in claim 1 wherein, the antifungal agents are azoles, clotrimazole, mystatin, amphotericin and similar materials.
10. A composition as claimed in claim 1 wherein fungi covering infections are mycetial, candida, yeast or other fungicidal compounds.
11. A composition as claimed in claim 1 wherein, the living system are bacteria, fungi or any living cells.

12. A composition as claimed in claim 1 wherein the concentration of the cow urine (*Go-mutra*) distillate is in the range between 0.001 µl/ml to 100 µl/ml.

13. A composition as claimed in claim 1 wherein the cow urine (*Go-mutra*) enhances membrane permeability of molecules, drugs across the semi-permeable membrane and mammalian gut membrane, and is used for enhancing intestinal transport and transport of molecules across membranes of various biological functions.

14. A process of preparing powder (Gm-IV) from cow urine distillate , said process comprising:

    a. mixing cow urine distillate with half the volume of methanol and extracting with hexane.

    b. lyophilizing the hexane fraction (Gm-I) and testing for similar activity as that of cow urine (*Go-mutra*).

    c. extraction of the aqueous fraction with ethyl acetate and lyophilizing the ethyl acetate fraction (Gm-II) and testing for similar activity as that of cow urine (*Go-mutra*).

    d. further, extracting the aqueous fraction containing white precipitate with butanol and lyophilizing the butanol fraction (Gm-III) having pale yellow precipitate and testing for similar activity as that of cow urine (*Go-mutra*).

    e. drying the remaining aqueous fraction containing white crystalline precipitate (Gm-IV) and testing for similar activity as that of cow urine (*Go-mutra*).

15. A process as claimed in claim 14 wherein, the lyophilized extract Gm-IV from cow urine distillate is devoid of typical cow urine distillate smell.

16. A process as claimed in claim 14 wherein, the lyophilized extract Gm-IV is having the following properties.

    Color: White

    Physical state: Solid Crystalline

    Solubility: Water-soluble and mixtures containing water

    Melting point: Above 400°C

    Specific Gravity: 1.006

    RF value in methanol: Chloroform (50: 50) phase: 0.65

17. A process as claimed in claim 14 wherein, starting cow urine distillate is having HPLC properties having two major peaks with retention time 5.334 and 11.310 min.

18. A process as claimed in claim 14 wherein, the lyophilized extract possess all the activities like that of the distillate at a concentration in the range of 0.1 to 100 μg/ml, with much more stability at room temperature and solubility in water.

19. A lyophilized bio-active product obtained from cow urine distillate which is having the following physical characters:
Color: White
Physical state: Solid Crystalline
Solubility: Water-soluble and mixture containing water
Melting point: Above 400°C
Specific Gravity: 1.006
RF value in methanol: Chloroform (50: 50) phase: 0.65

20. A lyophilized product as claimed in claim 19 wherein, the bio-active product GM-IV is devoid of typical cow urine distillate smell.

21. A lyophilized product as claimed in claim 19 wherein, the bio-active product is used at concentration 0.1 to 100 μg/ml, with much more stability at room temperature and solubility in water.

22. A lyophilized product as claimed in claim 19 is used to enhance membrane permeability of molecules, drugs across the semi-permeable membrane and mammalian gut membrane, and can be used for enhancing intestinal transport and transport of molecules across membranes of various biological functions.

23. A composition comprising an effective amount of bioactive lyophilized fraction obtained from cow urine distillate, which is used as a bio-enhancer and bioavailability facilitator and one or more nutraceuticals, antibiotic, anti-infective, anticancer agents.

24. A composition as claimed in claim 23 wherein the bioactive fraction has enhancing activity of anti-bacterial agents, anti-cancer agents and anti-tuberculosis agents by 2 to 80 folds.

25. A composition as claimed in claim 23 wherein the anti bacterial agents are selected but not limited to from the group comprising Quinolones, Rifampicin, tetracycline, amphicillin and other similar agents.

26. A composition as claimed in claim 23 wherein the anti bacterial agent is an anti-tuberculosis agent selected from isoniazid, pyrazinamide, ethambutol and other similar compounds.

27. A composition as claimed in claim 23 wherein the bioactive fraction has enhancing activity of anti- tuberculosis agents by 2 to 20 folds.

28. A composition as claimed in claim 23 wherein the anti-cancer agent is selected from group consisting of Paclitaxel (Taxol).

29. A composition as claimed in claim 23 wherein the bioactive fraction has enhancing activity of anti- cancer agents by 2 to 20 folds.

30. A new use of cow urine distillate as a bio-enhancer and bioavailability facilitator of one or more nutraceuticals, antibiotics, anti-infective and anticancer agents.

31. A use as claimed in claim 30 wherein the anti bacterial agents are selected from the group comprising Quinolones, Rifampicin, tetracycline and ampicillin and similar compounds.

32. A use as claimed in claim 30 wherein, wherein the anti bacterial agent is an anti-tuberculosis agent selected from isoniazid, pyrazinamide, ethambutol and other similar compounds.

33. A use as claimed in claim 30 wherein, the anti-cancer agent is selected from group consisting of Paclitaxel (Taxol).

34. A use as claimed in claim 30 wherein, the cow urine distillate is used as bioavailability facilitator for anticancer therapy directly or in combination with anticancer molecules.

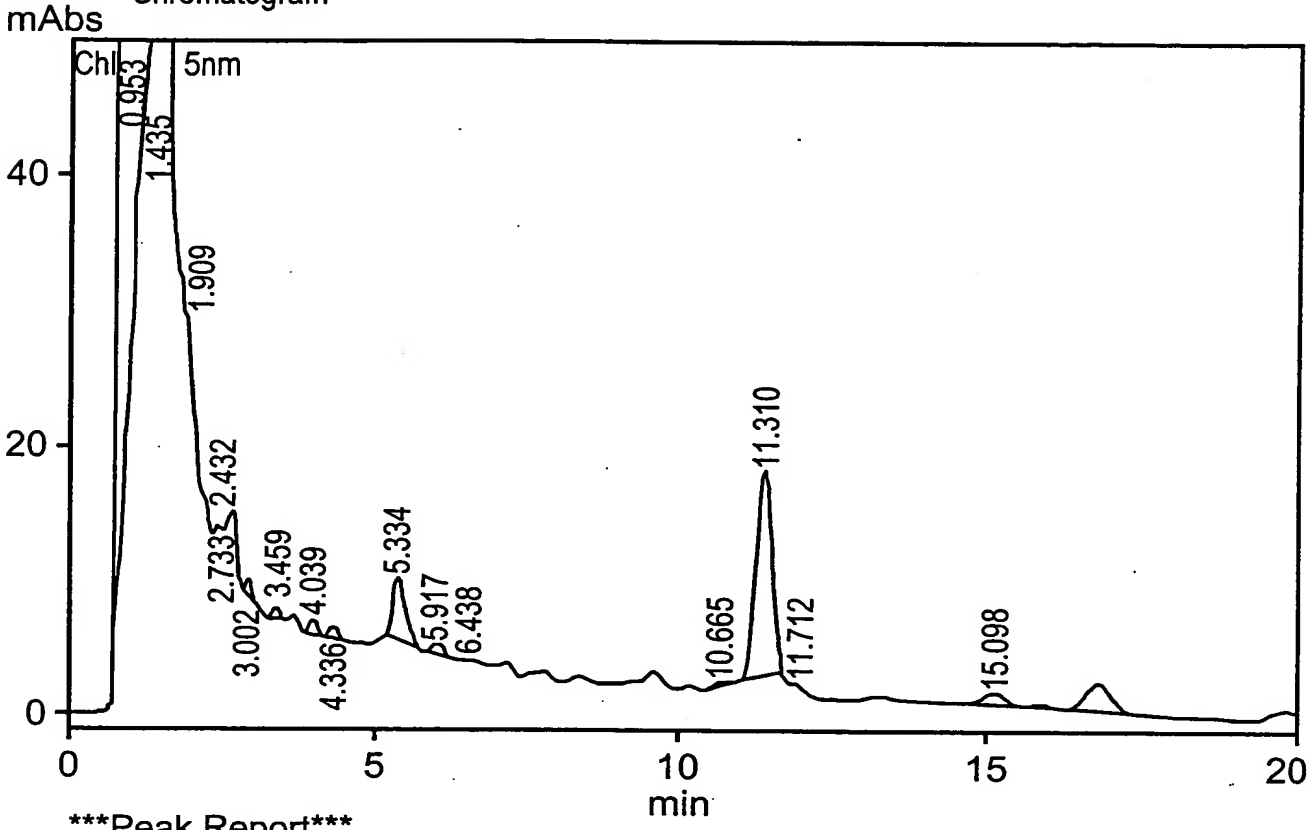
35. A use as claimed in claims 1-34 wherein, the concentration of the cow urine distillate and lyophilized powder is very critical and increased amount above the upper limit may mar the effect/activity in formulation or administered dosage.

ABSTRACT

The invention relates to a novel pharmaceutical composition comprising an effective amount of bio-active fraction from cow urine distillate as a bioavailability facilitator and pharmaceutically acceptable additives selected from anticancer compounds, antibiotics, drugs, therapeutic and nutraceutic agents, ions and similar molecules which are targeted to the living systems.

Sample
ID :
Type : Unknown
Detector : SPD-M10Avp
Operator :
Method Name : ANAL.MET

*** Chromatogram ***



Peak Report

PKNO	ChNO	TIME	AREA	MK	PURITY.UP	PURITY.DOWN	IDNO	CONC
1	1	0.953	9552712					78.9928
2	1	1.438	2027186					16.7631
3	1	1.909	7380					0.0610
4	1	2.432	2312					0.0191
5	1	2.733	26772					0.2214
6	1	3.002	11050					0.0914
7	1	3.459	5526					0.0457
8	1	4.039	9699					0.0802
9	1	4.336	9040					0.0748
10	1	5.334	59563					0.4925
11	1	5.917	11104					0.0918
12	1	6.438	2800					0.0232
13	1	10.665	4544					0.0376
14	1	11.310	265970					2.1993
15	1	11.712	2676					0.0221
16	1	15.098	94810					0.7840
			12093144					100.0000

FIG. 1